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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,406	04/11/2001	Ronald Erwin Boch	273012011300	3418

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,406	BOCH ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,23-29,31,41 and 46-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,23-29,31,41 and 46-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed on 1-15-04 is acknowledged.

Claims included in the prosecution are 21, 23-29, 31, 41, and 46-57.

In view of applicant's amendments, the 102 rejections are withdrawn.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 21, 23-29, 31, 41, 46-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madden (5,389,378) or Liu (5,707,608) or Desai (6,074,666), in view of applicant's statements of prior art.

As discussed before, Madden discloses phospholipid formulations containing BPD-MA, DMPC (saturated lipid) and PC (unsaturated lipid). The method of preparation involves the mixing the agents and the lipids, evaporation of the solvent and hydrating the film at 30 degrees (note the abstract, columns 5-8, Examples and claims).

Liu discloses phospholipid formulations containing the claimed green porphyrins, DMPC and PG. The compositions include an antioxidant. The method of preparation

involves the mixing the agents and the lipids, evaporation of the solvent and hydrating the film below 30 degrees and subjecting the mixture to high-speed homogenizer (micro fluidizer) (note the abstract, columns 6-12, Examples and claims).

Similarly, Desai discloses phospholipid formulations containing the claimed green porphyrins, DMPC and PG. The compositions include an antioxidant. The method of preparation involves the mixing the agents and the lipids, evaporation of the solvent and hydrating the film below 30 degrees (note the abstract, columns 3-7, Examples and claims).

What are lacking in these references are the teachings of the phospholipid composition in the form of micelles. Applicant on page 28 of the specification indicate that hydration to multilamellar vesicles followed by high energy processing step would result in the formation of micelles. Since the references teach the high energy processing steps, it would have been obvious to one of ordinary skill in the art that the compositions in the prior art would also contain micelles besides liposomes. Furthermore, if the formation of micelles were preferred, it would have been obvious to subject the phospholipid preparations to high energy processing steps till the formulations contain only micelles of desired sizes. It would appear that the references do not teach claimed porphyrin derivatives. Applicants in the specification indicate that the claimed derivatives are known in the art. The use of art known porphyrins in the liposomes of Madden or Liu or Desai, with the expectation of obtaining at least similar results, would have been obvious to one of ordinary skill in the art since these are photosensitizers with the same basic porphyrin structure.

Applicant provides no specific arguments to this 103 rejection and therefore, the rejection is maintained.

3. Claims 21, 23-29, 31, 41, 46-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madden or Liu or Desai cited above in view of either Lentini (5,885,557) or Young (6,375,930) in further combination with Wan (5,329029).

As discussed before, Madden discloses phospholipid formulations containing BPD-MA, DMPC (saturated lipid) and PC (unsaturated lipid). The method of preparation involves the mixing the agents and the lipids, evaporation of the solvent and hydrating the film at 30 degrees (note the abstract, columns 5-8, Examples and claims).

Liu discloses phospholipid formulations containing the claimed green porphyrins, DMPC and PG. The compositions include an antioxidant. The method of preparation involves the mixing the agents and the lipids, evaporation of the solvent and hydrating the film below 30 degrees (note the abstract, columns 6-12, Examples and claims).

Similarly, Desai discloses phospholipid formulations containing the claimed green porphyrins, DMPC and PG. The compositions include an antioxidant. The method of preparation involves the mixing the agents and the lipids, evaporation of the solvent and hydrating the film below 30 degrees (note the abstract, columns 3-7, Examples and claims).

What is lacking in Madden, Liu, and Desai are the explicit teachings of the formation of phospholipids in micellar form. Applicant on page 28 of the specification indicate that hydration to multilamellar vesicles followed by high energy processing step would result in the formation of micelles. Since the references teach the high energy

processing steps, it would have been obvious to one of ordinary skill in the art that the compositions in the prior art would also contain micelles besides liposomes. It would appear that the references do not teach claimed porphyrin derivatives. Applicants in the specification indicate that the claimed derivatives are known in the art. The use of art known porphyrins in the liposomes of Madden or Liu or Desai, with the expectation of obtaining at least similar results, would have been obvious to one of ordinary skill in the art since these are photosensitizers with the same basic porphyrin structure. Both Lentini, and Young discloses that photodynamic therapy could be practiced with photosensitizing material in carriers such as micelles and liposomes (note the abstract, col. 7, line 62 through col. 8, line 29 of Lentini; abstract, col. 11, line 33 through col. 13, line 43 of Young). Although Young discusses phospholipids, it is unclear whether he specifically advocates their use in the micelle formation. Wan discloses that phospholipids are amphiphilic in nature and have a propensity to form micelles and bilayers in an aqueous medium Col. 2, lines 3-5).

The use of phospholipids as micellar forming structures in Lentini or Young for the delivery of benzoporphyrins of Madden or Liu or Desai would have been obvious to one of ordinary skill in the art since phospholipids are known active agent carriers and the reference of Wan shows that they have the ability to form either liposomes or micelles upon the addition of an aqueous medium (col. 2, lines 3-5).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that in order to render a claimed invention obvious, the cited art not

only has to 1) teach or suggest every element of the claimed invention; 2) must also provide some suggestion or motivation to modify the references to arrive at the claimed invention and 3) there must be some reasonable expectation of success of such modification. It is the examiner's position that all of these conditions have been met by the combination of the references.

Applicant argues that Madden uses extrusion process to generate appropriate sized liposomes ranging from 100 to about 120 nm in diameter and that the extrusion process does not produce micelles. Applicant's arguments with regard to Liu and Desai are on similar grounds. These arguments are not found to be persuasive. A careful review of the specification indicates that applicants themselves are using art known liposome method of preparation steps such as aseptic filtration of the composition through 0.22 micron filters or micro fluidizers, sonicators, high-shear mixers and homogenizers (pages 35, 38, 43 and 45) which are the same as the methods employed by Madden, Liu and Desai. Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Lentini is directed to photodynamic treatment of the skin and mentions micelles along with liposomes and gels as formulations for use in sustained-release delivery of photosensitizing agent, psoralen. According to applicant Lentini does not teach or suggest micelles comprising saturated and unsaturated phospholipids. These arguments are not found to be persuasive since from the prior art, it is evident that both micelles and liposomes can be made from phospholipids containing saturated or unsaturated fatty acid chains or both. Though Lentini does not teach how to make the micelles or liposomes, he teaches that these

are sustained release preparations and can be used in photodynamic therapy. Lentini also teaches other modes of administration including oral besides topical administration.

Applicant argues that Young is limited to the use of texaphyrins, which are distinct from the hydro-monobenzo-porphyrin photosensitizers. This argument is not found to be persuasive since Young shows the ability of phospholipid micelles to encapsulate active agents and this ability of micelles to encapsulate any agent will be the same and applicant has not shown that to be otherwise. Furthermore, the primary references which teach the encapsulation of porphyrins in liposomes which are made by phospholipids which have the ability to form micelles also. The examiner has established motivation to use micelles and the reasonable expectation of success and applicant has not shown any unexpected findings resulting from the use of phospholipids in the form of micelles instead of liposomes in the delivery of photoporphyrins. In fact, the reference of Madden establishes surprisingly high drug to lipid ratios can be achieved with BPD-MA and BPE-MB using the phospholipids in the form of liposomes (col. 5, line 5 et seq.).

The examiner cites the following as the state of the art:

5,879703 which refers to micelles as "liposome structures such as micelles, multilamellar vesicles and unilamellar vesicles";

4946683 and 5,435989 which refer liposomes as 'liposome micellar particles" and 5,320906 and 4,753,788 which refer to liposomes as "phospholipid micellar particles in the form of unilamellar and multilamellar vesicles.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.

Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK